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NATURE AND CONTROL OF HEMORRHAGE IN NASO-PHARYNGEAL OPERATIONS.*

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The operative technique in nasopharyngeal work has recently seen such gradual and progressive improvement that the procedures involved have at the present time reached a high degree of efficiency. Indeed, numerous methods offer themselves to the specialist in this field of surgery, and it is the ability to choose and execute the one procedure specially adapted to the exigencies of the case on hand that marks the man with extensive and varied experience in nasopharyngeal work, that is, the specialist, from the occasional operator on the nose and throat.

Such rapid progress in operative technique has had, however, one undesirable feature. It has somewhat blunted the recognition of the fact that nasopharyngeal operations are in many ways similar to the major operations of surgery, involving comparable risks from shock, anesthesia, infection, etc.

Moreover, the one striking thing about a major operation is its comparative bloodlessness, and the great care taken to effect such bloodlessness to the highest degree possible. In nasopharyngeal work, on the other hand, much remains to be done in this phase of the operation to obtain any results that are comparable to those attained in general surgery. Yet, careful comparison of a laparotomy with a tonsillectomy, let us say, shows that the dangers of uncontrolled hemorrhage or oozing is rather more marked in the latter than in the former. Of course, bleeding from a large vessel is equally dangerous whether the blood enters the peritoneal cavity or gushes from the mouth, and its treatment, that is, ligation of the large vessels is equally imperative and is about the same in procedure in either case.

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On the other hand, smaller hemorrhages in our work are of greater significance because the blood is apt to enter the bronchi and the lungs with much more serious consequences than if the free peritoneum were involved. Moreover, such blood is more apt to be and indeed almost always is mixed with infected tissues or secretions, for, of course, no nasopharyngeal field can be made as sterile as a clean peritoneal or other field of surgical interference. To the dangers of mechanical damage due to interference with respiration and with the circulation in the lungs, is added the probability of infection with all its dire consequences from a slight bronchitis to a bronchopneumonia or a lung abscess. In this connection the great difficulty of immobilizing the site of bleeding in nasopharyngeal work, the site of operation being usually involved in the movements of respiration, swallowing, vomiting, etc., must be remembered and compared with the more or less greater ease with which other fields may be immobilized from the complete rest of an extremity to the fairly complete paralysis of the intestine attainable by the use of drugs.

Still there is no denying the fact that nasopharyngeal operations are done by the hundreds in which these considerations are hardly entered into, and it is probable that it is merely the lack of such records as are usually available in the major surgical field that hide the fact of the extensive amount of damage that results. There seems to be no reason why progress in this important detail of operation should not go on at a speedier rate than heretofore has been the case. Careful study of the literature and extensive experience in special nasopharyngeal work have convinced the writer that there has been rather a lack of application of the various methods involved rather than absence of remedies dealing with the evil.

The procedures involved in dealing with nasopharyngeal hemorrhage are preventive, surgical and medical. The preventive methods in the first place depend upon such study of the general condition of the patient as may reveal any constitutional conditions favoring a hemorrhage from the much feared hemophilia to diseased kidneys with consequent high blood pressure. Such study we may safely leave to the internist or to the family practitioner who is usually the intermediary between the patient and the specialist surgeon. I would like to warn the latter, however, from taking any unnecessary risks in the matter with patients who reach him directly or in whom the general examination has not been thoroughly performed. The time spent in having such examination done while apparently thrown away in case after case, may save him from the great misfortune of witnessing a serious or fatal outcome after operation upon a patient who should either never have come to operation or have been properly prepared for the procedure.

Further prevention is inherent in such mastery of technique as shall result in the choice of the method best adapted to the individual case. In this connection, the recent anatomical studies of Balatnikow[1] are interesting. He says: "The topographical relations between the large vessels and the lateral pharyngeal wall are dependent, in a great measure, upon the development of the bony parts of the skull in that region, and that on account of the poor development of the visceral portion of the skull, the blood vessels lie closer to the tonsils in adults than in children."

The position of the head had an influence on the topography of the vessels and their relation to the tonsils; the blood vessels are closer to the lateral pharyngeal wall on that side from which the head is turned away and further away on the opposite side.

The distance between the tonsils and the internal carotid is about one-half to one centimeter, and between the tonsil and the external carotid artery is about two centimeters. This distance, however, is variable. Opening the mouth and depressing the tongue was found to have no influence on the position of the blood vessels in the dead body, but in the living it is possible, by such manoeuvers, to bring about a change in the position of the vessels, particularly if there is an infiltration of the peritonsillar tissue. The pharyngeal wall is in intimate relation with the internal and external carotid arteries, the facial, the lingual, and the ascending palatine artery, and sometimes with the ascending pharyngeal artery and also with the submucous peripharyngeal plexus of veins. The "bouquet of Riolan," a cluster of ligaments and muscles attached to the styloid process, cannot always be relied upon as a protection to the blood vessels, as their relation is dependent upon the height of the cut.

Speaking about hemorrhages, Balatnikow says: "Hemorrhage following operation on a peripharyngeal abscess may come either because the arteries are wounded or because the veins are distended or varicose. As the arterial branches reach the tonsil capsule only, breaking up into capillaries on entering the tissues of the tonsil, tonsillotomy should not be followed by more than capillary or venous bleeding. If the tonsil, however, is completely removed within its capsule, severe arterial bleeding is possible. Because of the possibility of an abnormal position of the blood vessels, they should be carefully located by palpation before operating."

The following rules for operation are laid down by Balatnikow:

"In tonsillotomy, only that portion of the tonsil which projects into the throat should be removed. The tonsils should never be pulled out of their niche and the instrument should never be pressed hard against the lateral wall of the pharynx.

"In pharyngeal abscess, all precautions should be taken to check possible bleeding—instruments to sew the pillars or even to ligate the common carotid artery being held ready.

"The patient's head should be firmly fixed, the medium position being suggested as the one most desirable both from the standpoint of danger and facility in operating.

"The knife should only be used in making the incision through the mucous membrane, all deep exploration being done with a dull instrument. The wound should not be carried more than a centimeter and a half deep if a sharp pointed instrument is used.

"The surface of the cut should be parallel with the long axis of the mouth and the knife must never be directed backward and outward. The site of the incision be determined according to Thompson, i. e., the wound should be made in the apex of the external inferior quadrant, which is determined by drawing a line horizontally through the base of the uvula to meet a line drawn vertically through the anterior edge of the anterior faucial pillar."

The following hemostatic measures should be employed in the order given in cases of post-operative hemorrhage following operation upon the tonsils and lateral wall of the pharynx.

(1) Application of Mikulicz's compression forceps;
(2) Sewing together of the palatal arches;
(3) Compression of the common carotid artery;
(4) Ligation of the common carotid artery or its branches.

J. Leslie Davis'[2] investigations concerning the blood supply of the tonsils are also of interest. He says: "There are certain fixed sources of all hemorrhages from tonsillectomy operations and the majority of the text books are in error as to the blood supply of the tonsils." The entire supply comes from one artery which is formed "by an anastomosis of the ascending palatine branch of the facial and the descending branch of the internal maxillary. The artery thus formed, enters the fossa at its superior extremity, passes downward through the capsule for a distance of about one-half an inch before penetrating the capsule to reach the tonsil parenchyma." The tonsillar branch of the facial artery, the branch from the dorsalis lingua, and the branch from the ascending pharyngeal, supply only the surrounding structures in 95 per cent of cases at least. Davis, therefore, after enucleation of the tonsil places a suture ligature (using No. 1 catgut) around this artery in the upper part of the tonsillar fossa and ties it off. This is his routine practice in all adult cases, but with children, only when the bleeding is profuse and continuous.

While some of the conclusions drawn by the above investigators may be open to criticism, it is the purpose of this paper to call your attention to the amount and character of the work that has been done rather than to its merits or demerits.

Based upon the commonly accepted causes of hemorrhage, viz., high blood pressure, persistent vaso-dilatation and delayed blood clotting, therapeutic measures employed in the control of hemorrhage are of three kinds:

(1) Those equalizing the circulation and lessening the intravascular pressure at the bleeding point;

(2) Those contracting the vessel itself;

(3) Those decreasing the coagulation time of the blood.

Recent investigations of the phenomena of clotting of the blood have shown that normal blood in itself contains substances which, under certain conditions, unite to bring about coagulation.

According to Morawitz, a substance which he calls thrombokinase is present in all body tissues and especially in blood platelets. Prothrombin, antithrombin, calcium salts and fibrinogen are constantly present in normal blood. When the tissues or formed elements of the blood are injured, thrombokinase combines with the calcium salts and prothrombin to produce a new substance called thrombin which, with the fibrinogen forms fibrin or clot.

According to the investigations of Bordet and LeLange, thrombin is formed by the reaction between cytozyme and serozyme in the presence of a calcium salt. The cytozyme is found in platelets, leucocytes, and tissue juices (probably the thrombokinase of Morawitz and Howell) and the serozyme in the blood serum. These investigators attribute the formation of fibrin to the action of thrombin on fibrinogen.

Howell assumes that while the elements of coagulation are all present in the blood, there is normally sufficient antithrombin to prevent clot formation. The balance between the two is very delicate; cellular injury releases a substance, which he calls thromboplastin, that neutralizes or binds the antithrombin and permits the other elements of the blood to combine in the formation of the clot. Howell's views seem to explain the known phenomena of coagulation more completely than the earlier theories.

While we cannot enter into a detailed review of these studies, the theories of the formation of antithrombin must be mentioned as being of great interest and importance in the intelligent understanding of the factors underlying operative hemorrhage.

Most investigators agree that antithrombin is formed in the liver. Experiments on the origin of antithrombin have been carried on with few exceptions with Witte peptone which, when injected intravenously into dogs produces an anticlotting substance in the blood. That the liver is at least a factor in the production of antithrombin has been shown by the discovery that in dogs in which the liver has been eliminated from the general circulation injections of peptone do not have an anti-clotting effect on the blood.

Denny and Minot[3] conducted a series of experiments to determine the antithrombin contents of the blood in different parts of the body and attempted to produce antithrombin. Their investigations included a study of the effect of liver destroying substances upon the antithrombin content of the blood and have led to the following conclusions:

Antithrombin is formed in the liver. Venous blood taken from the liver, spleen, kidneys and intestines shows no appreciable difference from the blood of the jugular vein in antithrombin content.

When stasis is produced in any of these organs the liver blood alone shows a definite increase in antithrombin.

Perfusion of the liver with defibrinated blood causes an increase in antithrombin in the perfusate. Perfusion of the head, spleen and hind leg shows no marked increase and generally a decrease in antithrombin content.

Attempts to stimulate the liver to production of antithrombin by means of bile, bile salts, secretin and electrical stimulation were negative. Injection of small amounts of thrombin into the portal circulation caused a slight rise in antithrombin.

Dogs with phosphorous poisoning and consequent liver destruction show a marked increase in antithrombin content of the blood as well as a diminution in fibrinogen.

An interesting paper by Katherine and Cecil Drinker[4] on the effect of rapid progressive hemorrhage on the coagulation time of blood was published in February, 1914. According to these investigators, such hemorrhage causes a decrease in coagulation time, a gradual steady fall being noticeable as hemorrhage proceeds. This change was accomplished by a decrease in antithrombin, its amount remaining constant when the coagulation time was unchanged. Prothrombin was shown to increase slightly at first and then to decrease slightly. Fibrinogen was found to decrease as hemorrhage progressed. Platelet counts did not vary with progressive hemorrhage.

Gray and Lunt[5] conclude that moderately severe hemorrhage (13 per cent of the circulating blood) decreases clotting time. The important coagulating factors may be localized in the abdomen because (1) exclusion of the abdominal circulation increases clotting time and (2) hemorrhage after exclusion no longer results in decrease of clotting time.

The adrenal glands probably favor by their secretion rapid clotting after hemorrhage, but after adrenalectomy hemorrhage still decreases the clotting time.

Exclusion of the intestines usually increases clotting time but after this exclusion, hemorrhage can still decrease the clotting time.

The important role which the liver has been proved to play in coagulation indicates that it provides, perhaps in coöperation with the intestines and the adrenal glands, the necessary elements to hasten clotting after extensive bleeding.

Vosburgh and Richards[10] in 1903 noticed that an increase in sugar content caused the blood to coagulate more rapidly and as they had obtained this result by painting adrenalin on the pancreas, concluded that this was due to the action of adrenalin on the pancreas. Wiggers, a few years later discredited this. Von den Velden[11] in 1911 asserted that adrenalin decreased the coagulation time in man about one-half but attributed it to vasoconstriction which caused a discharge of tissue juices into the blood.

Cannon and Gray[6] discredit the theories of both Vosburgh and Richards and of Von den Velden and conclude that:

Adrenalin injected in small doses intravenously (0.001 mg. per kilo) and in large doses subcutaneously, will shorten coagulation time to one-half or one-third the former duration. The prompt shortening of the process after small doses is changed after larger doses (about 0.03 mg. per kilo) to a lengthening and later a shortening, or to a lengthening alone.

The effect of adrenalin on the clotting time is not associated with any corresponding effect on arterial pressure.

If the blood is confined anterior to the diaphragm, or if the intestines and liver are removed, adrenalin in small doses does not cause rapid clotting.

The addition of small amounts of adrenalin to drawn blood does not hasten clotting. Increase of dextrose in the blood to 0.3 or 0.4 per cent does not cause the rapid clotting seen after adrenalin injection.

The explanation is suggested that adrenalin accelerates the clotting process by stimulating the liver and perhaps the intestines to greater activity in discharging some factor or factors in coagulation.

In the same year Cannon and Mendenhall,[7] using as a basis for their experiments the discovery that injected adrenalin shortened the coagulation time of blood, attempted to increase the secretion of the adrenals by stimulating the splanchnic nerves to produce similar effects with the following results:

Stimulation of the splanchnic nerves results immediately or after a brief delay in shortening the coagulation time of blood.

Such stimulation usually produced less marked effect as it is repeated. If the adrenal gland is removed on one side, splanchnic stimulation on that side does not shorten clotting time; whereas splanchnic stimulation on the other side is still effective. The faster clotting is therefore due to increased adrenal discharge.

Since stimulation of the nerves supplying the liver and intestines does not hasten clotting and since increase of adrenalin has no effect in the absence of the liver and intestines, the shortened clotting after splanchnic stimulation is accounted for by the action of adrenal discharge on the liver and perhaps the intestines.

In a study on the effects of pain and emotional excitement upon coagulation of the blood, these investigators conclude that:

Stimulation of afferent nerves (sciatic, crural) or major operations under light anesthesia markedly shorten the coagulation time of blood. Emotional excitement is the occasion for very rapid clotting which becomes slow when the splanchnic nerves are cut. Pain and strong emotions have been proved to evoke secretion of the adrenal glands; and adrenalin hastens clotting. Rapid coagulation may be reasonably considered, therefore, as another instance of adaptive reaction serviceable to the organism in the injury which may accompany pain or which may follow the struggle that fear or rage may occasion.

Before concluding this part of my paper, I wish to call your attention to some recent investigations on the effects of chloroform and ether on the coagulation of the blood. In July, 1915, Mendenhall published a report of his investigations on this subject from which he draws the following conclusions:

Coagulation time is little altered by chloral hydrate.

Coagulation time is affected by chloroform as by chloral hydrate. The effects of chloral hydrate and chloroform are probably the result of disturbance and consequent interaction between two or more organs which are important in the coagulation process; probably liver, intestines and adrenal glands.

The evidence is not sufficient to prove that a retarding agent is produced.

Coagulation processes are hastened by ether anesthesia. The effect of ether is exerted wholly through its action upon the adrenals.

In December, 1915, Minot[8] summarized his investigations as follows:

Antithrombin is rendered inactive by choloroform and ether, thus allowing free thrombin, if present in an oxalated plasma, to clot fibrinogen.

Prothrombin is not converted to thrombin by chloroform; chloroform can precipitate both fibrinogen and prothrombin from an oxalated plasma. Chloroform does not weaken the action of a solution of pure thrombin. Ether does slightly.

Antithrombin could not be recovered from chloroform or ether extracts of serum or plasma, unheated or heated to 60 degrees C., and is not exactly identical to antitrypsin or to Doyan's antithrombin.

In one chloroform poisoned rabbit, the antithrombin of the blood was decreased below normal.

With the conclusions of these and other investigators in the field of physiology in mind, other scientists in the fields of bio-chemistry and pharmacology, have been at work with the idea to strengthen and hasten by therapeutic means the natural processes of coagulation. I shall mention a few of the better known products which have been the result of their efforts.

Immediately after Oliver and Schaefer, and Czybulski and Szymonivicz discovered in 1895 that there was a very marked rise in blood pressure after intravenous injections of extracts of the suprarenal glands, Moore demonstrated "that the active substance was only present in the medullary portion of the gland and that it was identical with a chromogenic substance, described by Vulpian as early as 1856, possessing striking color reactions—green coloration with iron chloride on the addition of alkalies or with iodin or chlorin water a pink-carmine color. The reaction suggested brenzcatechin and Von Furth succeeded in preparing from this chromogen a substance which in its behavior agreed with brenzcatechin. Takamine first prepared the crystallized active substance in 1901 and named it adrenaline." (Meyer and Gottlieb.) To discuss further so widely and well known a substance as adrenalin would be superfluous.

In 1867, Pelletier separated from ipecacuanha its emetic principle which he named emetine. In 1894, Paul and Cownley isolated its two crystalline alkaloids emetine and cephaeline. The uses to which this drug has been put are also well known. My personal experience with emetine in nasopharyngeal hemorrhage has been extremely gratifying and while I am unable to say in what manner it acts, I have come to look upon the injection of one-half grain of emetine before operation as a routine procedure in my operative work. I made a close study of my results when I first began to use emetine using the Duke's coagulometer in making my tests. My results after several months' experience warrant me in claiming that by a hypodermatic injection of one-half grain of emetine fifteen minutes before making my tests, I am able to reduce the bleeding time by one-third at least.

Pituitrin is described as an extract made from the infundibular portion of the hypophysis.. In 1913, Citelli published a report of his gratifying experiences with pituitrin in the control of nasopharyngeal hemorrhage and since then there have been other reports of a similar character. I tried out pituitrin in the same manner as I did emetine and obtained practically the same result, i. e., the bleeding time was reduced about one-third. I did not, however, get as uniform results as I did with emetine.

Coagulen Ciba was discovered by Professor Kocher of Berne University and his assistant, Dr. Anton Fonio, and is described by them as an extract of blood platelets containing cytozym which when added to animal blood combines with serozym existing in the blood and forms thrombin or fibrin ferment. Being wholly within the bounds of a physiological process, coagulation with this preparation is claimed to be harmless and non-irritating.

Fonio has published his personal experience in the treatment of 700 cases and says that in no case was any septic effect observed. Kausch, after treating 300 cases with coagulen ciba confirmed Dr. Fonio's experience, as also did Dr. Obermueller after an extensive use of it in rhinological practice. My own experience with this product has not been as extensive as with the two former preparations but in every case in which I have used it, it has shortened the bleeding time, in a number of instances having had an almost instantaneous effect.

Thromboplastin (tissue juice) is prepared from the liver and brain of cattle. Dr. Hess[9] published his preliminary report of his experiences with this tissue juice in April, 1915, and since that time, other reports have been made of its successful use in the control of hemorrhage.

Dr. John T. Cronin of the New York Department of Health, reports on its use as follows:

"The use of thromboplastin has been extended to all Department of Health Nose and Throat Clinics. In a summary of 2,036 tonsil and adenoid operations the results were all excellent, in a large majority of the cases there was no bleeding at all and in the remaining cases only slight bleeding. There were no bad after effects. In no case has the operator or nurse been obliged to return to the clinic to care for a bleeder since the use of thromboplastin has been made a routine procedure."

In the comparatively few cases in which I have used thromboplastin, I have had uniformly good results.

Coagulose, a product obtained by precipitating normal blood and said to contain the fibrin ferment necessary for clotting blood is reported to have given good results in nasopharyngeal hemorrhage. Frey in 1898, treated hemorrhage with normal horse serum. Weil reports a case in which he shortened the coagulation time from four and one-half hours to forty minutes by means of this treatment.

Still other products have been offered from time to time for the control of hemorrhage but have not become so well known and their effect has not been, consequently, so closely studied.

I have attempted to show that recent investigations by anatomists, physiologists and pharmacologists have a direct bearing upon the daily problems of our work and it is no less than imperative that the results obtained by these workers should find prompt application and control in actual operative technique. Such course of action must require a somewhat different attitude to nasopharyngeal surgery from that usually encountered. As I have shown, even the single element of hemorrhage presents as perplexing problems as any that may arise in the usual procedures of major surgery, and it demands the same attitude from us, workers in this special field, as the pioneer surgeons and the present leaders of surgical science have shown in their work.

Such attitude and with it success in the development of this important branch of medical endeavor must rest upon the following factors:

Careful study of the local anatomical situation and the discovery of facts leading to the improvement of general technique and especially improvements in the prevention and treatment of hemorrhage;

General examination of the patient with the purpose of discovering any constitutional or morbid factors leading to the decrease in the clotting index of the blood;

The choice of proper anesthetic and its proper administration.

The study of new substances developed in the laboratory and applicable in the diminution of the tendency to bleeding and in checking such hemorrhage once it has set in,

And, finally, such coöperation between the different workers in these varied fields as shall most certainly and quickly lead to our goal, that is, the proper and efficient correction of morbid conditions of the throat and nose, attained with least discomfort and danger to the patient.

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7. CANNON AND MENDENHALL: *Amer. Jour. Physiology*, July, 1915, p. 33.
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